

Case No. 21036YP

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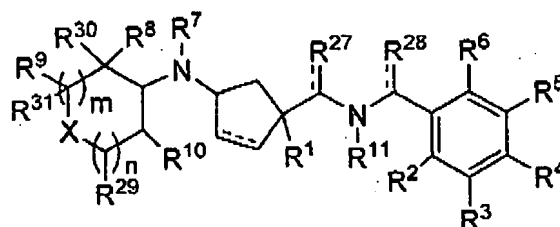
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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-O-, -NR²⁰-, -S-, -SO-, -SO₂-, and -CR²¹R²²-, -NSO₂R²⁰-,
-NCOR²⁰-, -NCO₂R²⁰-, -CR²¹CO₂R²⁰-, -CR²¹OCOR²⁰-, -CO-, -O-C(CH₃)₂-O-,

where R²⁰ is selected from: hydrogen, C₁-6 alkyl, benzyl, phenyl,

C₃-6 cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C₁-3alkyl, C₁-3alkoxy, -CO₂H, -CO₂-C₁-6 alkyl, and trifluoromethyl,

where R²¹ and R²² are independently selected from: hydrogen, hydroxy,

C₁-6 alkyl, -O-C₁-6alkyl, benzyl, phenyl, C₃-6 cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C₁-3alkyl, C₁-3alkoxy, -CO₂H, -CO₂-C₁-6 alkyl, and trifluoromethyl;

R¹ is selected from:

-C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl, -C₀₋₆alkyl-S-C₁₋₆alkyl,
 -C₀₋₆alkyl-SO₁₋₂-C₁₋₆alkyl, -C₀₋₆alkyl-SO₂-NR²⁶-C₁₋₆alkyl, -(C₀₋₆alkyl)-
 (C₃₋₇cycloalkyl)-(C₀₋₆alkyl), hydroxy, -CO₂R²⁰, heterocycle, -CN, -
 NR²⁰R²⁶, -NR²⁶SO₂R²⁰, -NR²⁶COR²¹, -OCOR²⁰, and phenyl,

where R²⁶ is selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl, C₃₋₆ cycloalkyl

where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and ~~trifluoromethyl~~ trifluoromethyl.

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7

substituents where the substituents are independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -CO₂R²⁰, -SO₂R²⁰, -NHCOCH₃, -NHSO₂CH₃, -heterocycle, =O, and -CN,

and where the phenyl and heterocycle are unsubstituted or substituted with 1-3

substituents where the substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

R² is selected from: hydrogen, C₁₋₆alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R³ is selected from: hydrogen, hydroxy, halo, C₁₋₆alkyl, -O-C₁₋₆alkyl, -NR²⁰R²¹, -NR²⁰CO₂R²¹, -NR²⁰CONR²⁰R²¹, -NR²⁰-SO₂-NR²⁰R²¹, -NR²⁰-SO₂-R²¹, heterocycle, -CN, -CONR²⁰R²¹, -CO₂R²⁰, -NO₂, -S-R²⁰, -SO-R²⁰, -SO₂-R²⁰, and -SO₂-NR²⁰R²¹;

R⁴ is selected from: hydrogen, C₁₋₆alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R⁵ is selected from: C₁₋₆alkyl substituted with 1-6 fluoro and optionally substituted with hydroxyl, -O-C₁₋₆alkyl substituted with 1-6 fluoro, -CO-C₁₋₆alkyl substituted with 1-6 fluoro, -S-C₁₋₆alkyl, -pyridyl, fluoro, chloro, bromo, and phenyl;

R⁶ is selected from: hydrogen, C₁₋₆alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R⁷ is selected from: hydrogen, C₁₋₆alkyl, and trifluoromethyl;

R⁸ is selected from: hydrogen, C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C₁₋₃alkoxy, hydroxy, -CO₂R²⁰, fluoro, -O-C₁₋₃alkyl, where alkyl may be unsubstituted or substituted with 1-3 fluoro, and C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, hydroxy, -CO₂R²⁰, -OCOR²⁰, and phenyl,

or R⁷ and R⁸ may be joined together via a C₂₋₄alkyl or a C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;

R⁹ is selected from: hydrogen, C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C₁₋₃alkoxy, hydroxy, -CO₂R²⁰, CO₂R²⁰, hydroxy, and -O-C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C₁₋₃alkoxy, hydroxy, and -CO₂R²⁰,

or R⁸ and R⁹ may be joined together by a C₁₋₄alkyl chain or a C₀₋₃alkyl-O-C₀₋₃alkyl chain to form a 3-6 membered ring;

R¹⁰ is selected from: hydrogen, and C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C₃₋₆cycloalkyl, and -O-C₁₋₃alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro,

or R⁸ and R¹⁰ may be joined together by a C₁₋₃alkyl chain or a single bond to form a 3-6 membered ring; where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO₂R²⁰, C₁₋₃alkyl, and C₁₋₃alkoxy,

or R⁸ and R¹⁰ may be joined together by a C₁₋₂alkyl-O-C₁₋₂alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO₂R²⁰, C₁₋₃alkyl, and C₁₋₃alkoxy,

or R⁸ and R¹⁰ may be joined together by a -O-C₁₋₂alkyl-O- chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO₂R²⁰, C₁₋₃alkyl, and C₁₋₃alkoxy;

R¹¹ is selected from: hydrogen, C₁₋₆alkyl, and trifluoromethyl;

R²⁷ and R²⁸ are independently selected from: =O, where R²⁷, R²⁸, or both, is oxygen and is connected via a double bond, hydrogen, phenyl, and C₁₋₆alkyl which may be substituted or unsubstituted with 1-6 of the following substituents:

-COR¹¹, hydroxy, fluoro, chloro, and -O-C₁₋₃alkyl;

R^{29} , R^{30} , and R^{31} are independently selected from: hydrogen, methyl, hydroxyl, trifluoromethyl, methoxy, and trifluoromethoxy;

or R^{29} and R^9 are connected by a C_{1-3} alkyl bridge;

m is selected from 0, 1, and 2;

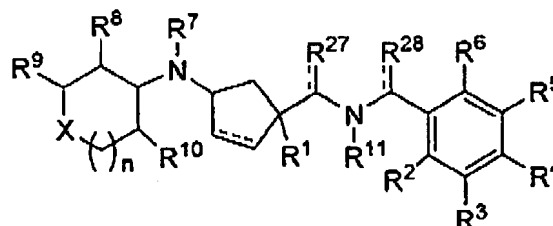
n is selected from 0, 1 and 2; and

the dashed line represents a single or a double bond;

and or a pharmaceutically acceptable salt salt thereof, ~~and individual diastereomers thereof.~~

2. (currently amended)

The compound of Claim 1 of the formula Ia:



Ia

and or a pharmaceutically acceptable salt ~~salts and individual diastereomers thereof.~~

3. (currently amended)

The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of: -O-, and -CH₂-.

4. (currently amended)

The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein X is -O-.

5. (currently amended)

The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from:

- (1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, and trifluoromethyl,

- (2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl,
- (3) -C₀₋₆alkyl-S-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl, and
- (4) -(C₃₋₅cycloalkyl)-(C₀₋₆alkyl), which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, and trifluoromethyl.

6. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R¹ is C₁₋₆alkyl which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: hydroxy, and fluoro.

7. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:
R¹ is selected from: isopropyl, -CH(OH)CH₃, and -CH₂CF₃.

8. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:
R² is selected from: hydrogen, hydroxy, and trifluoromethyl.

9. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:
R² is selected from: hydrogen, and hydroxy.

10. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

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R³ is selected from: C₁₋₆alkyl unsubstituted or substituted with 1-6 substituents
independently selected from fluoro, fluore, chloro, and bromo.

11. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

~~In the present invention it is more preferred that~~ R³ is selected from: ~~trifluoromethyl,~~
trifluoromethyl, cyclopropyl, and fluoro.

12. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

R⁵ is selected from: C₁₋₆alkyl unsubstituted or substituted with 1-6 substituents
independently selected from fluore, fluoro, chloro, and bromo.

13. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

R⁵ is selected from: ~~trifluoromethyl,~~ trifluoromethyl, cyclopropyl, and fluoro.

14. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein:

R⁵ is trifluoromethyl.

15. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R⁶ is hydrogen.

16. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R⁷ is hydrogen.

17. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^8 is selected from: hydrogen, C_{1-3} alkyl, which is unsubstituted or substituted with 1-6 fluoro, $-O-C_{1-3}$ alkyl, fluoro, and hydroxy.

18. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^8 is selected from: hydrogen, methyl, ethyl, trifluoromethyl, fluoro, and $-O-CH_3$.

19. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^9 is hydrogen and R^{10} is hydrogen.

20. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^8 and R^{10} are joined together by a $-CH_2CH_2-$ chain or a $-CH_2CH_2CH_2-$ chain to form a cyclopentyl ring or a cyclohexyl ring.

21. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^{27} is $=O$, where R^{27} is oxygen and is connected via a double bond.

22. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^9 and R^{29} are joined together by a C_{1-3} alkyl chain to form a ring.

23. (currently amended) The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^{29} is hydrogen, R^{30} is hydrogen, and R^{31} is hydrogen.

24. Canceled

25. (currently amended) A pharmaceutical composition which comprises an inert carrier and a the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

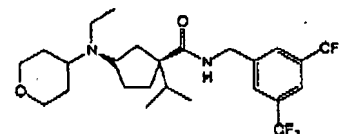
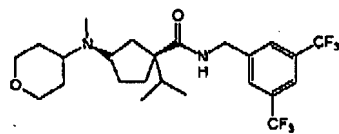
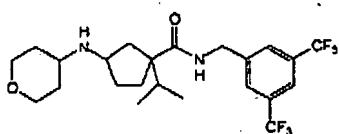
26. Canceled

27. (currently amended) A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

28. (currently amended) A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

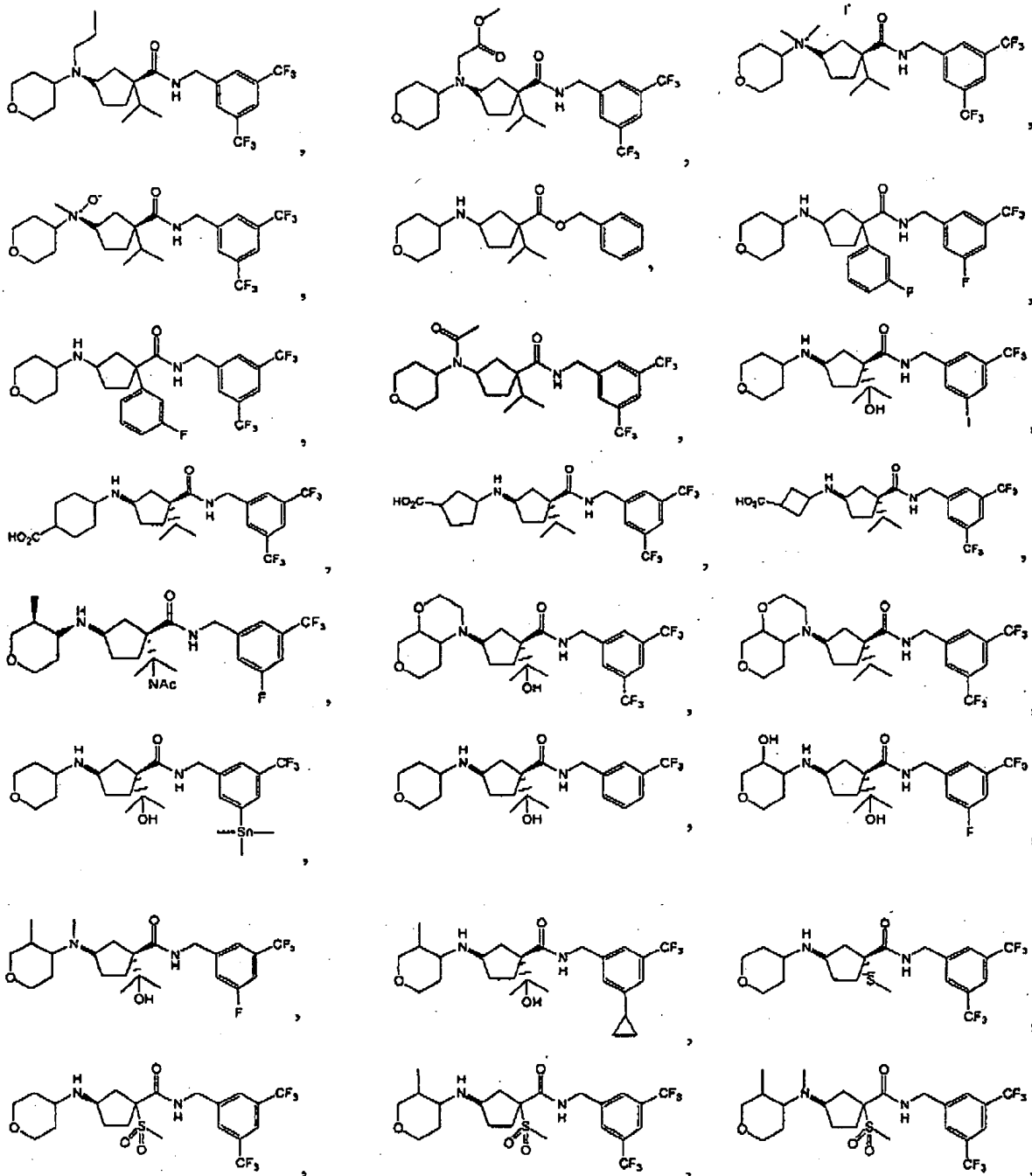
29. (currently amended) A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1, or a pharmaceutically acceptable salt thereof.

30. (previously presented) A compound which is selected from the group consisting of:



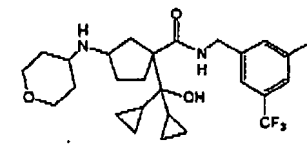
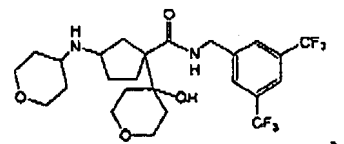
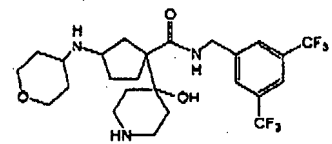
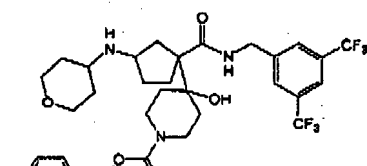
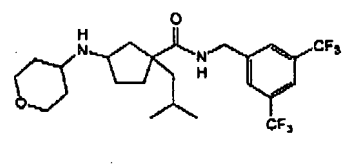
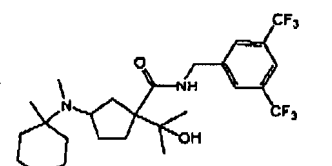
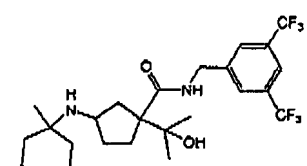
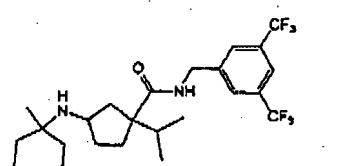
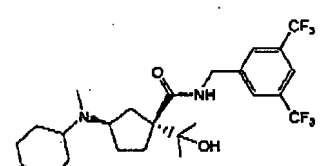
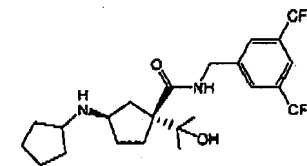
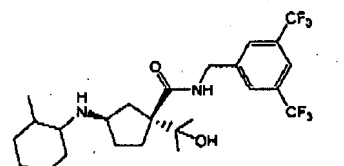
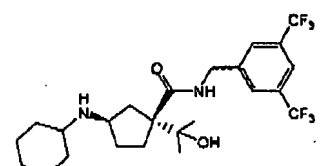
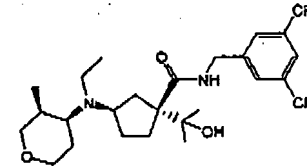
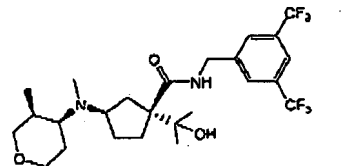
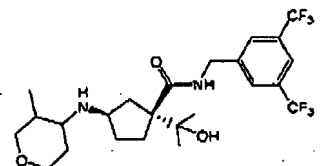
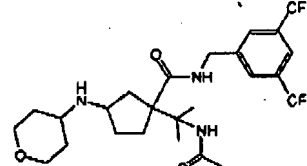
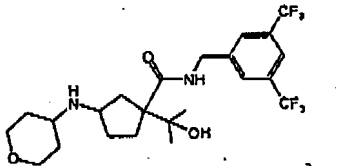
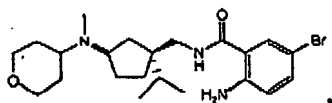
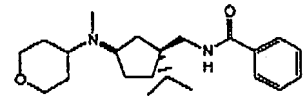
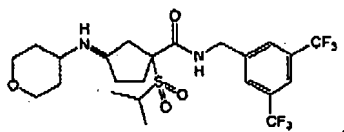
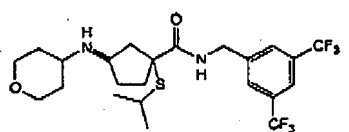
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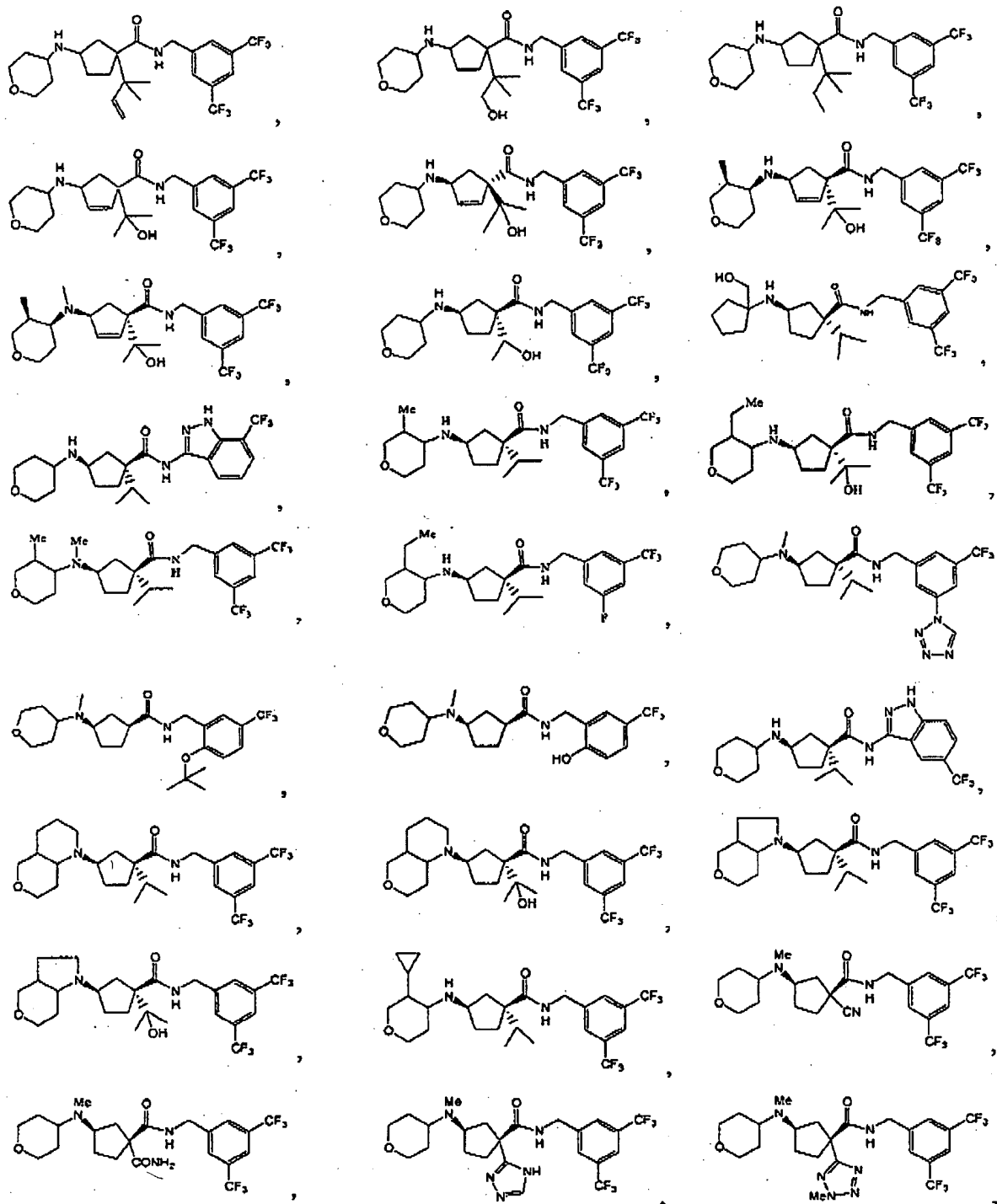
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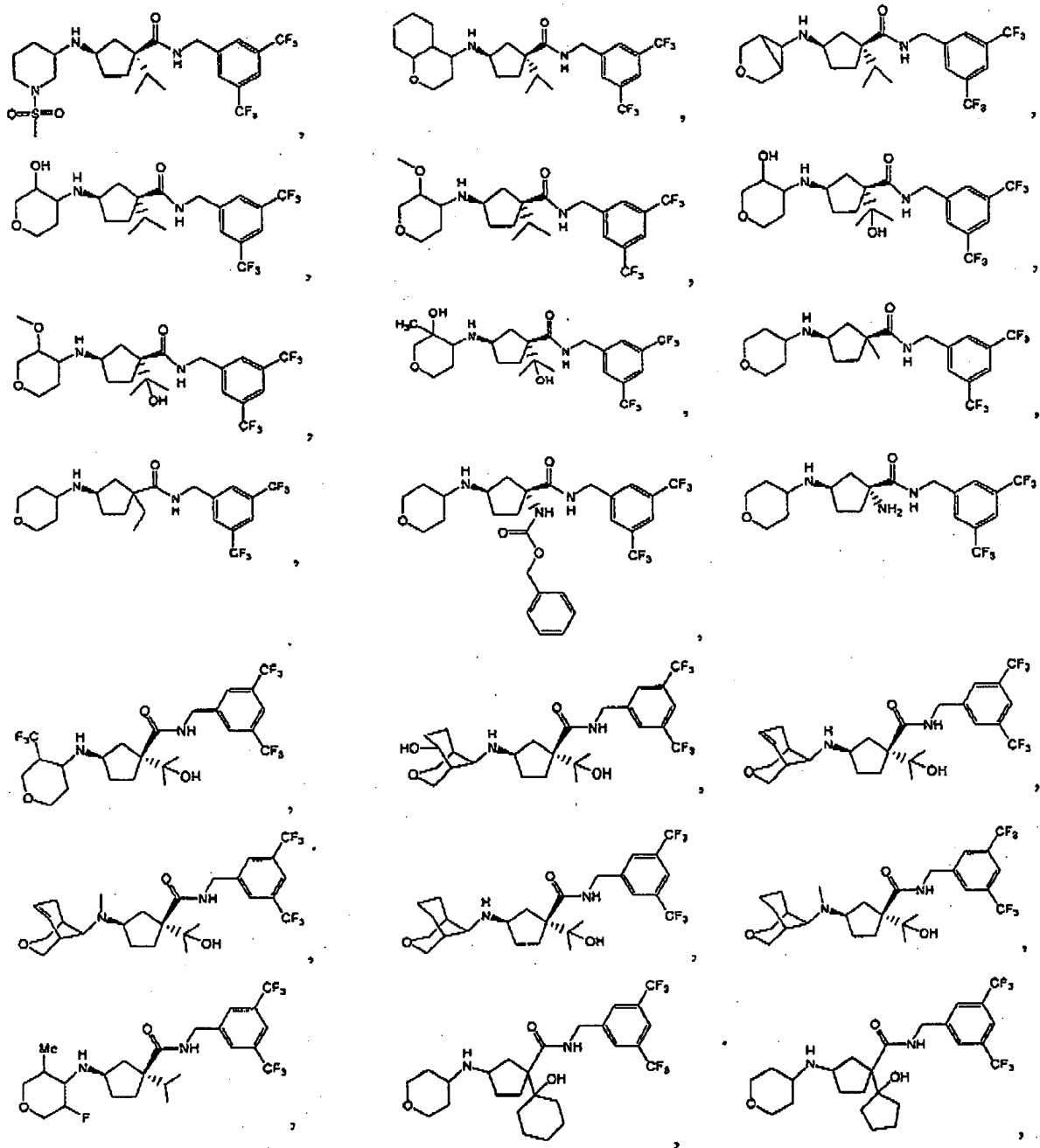
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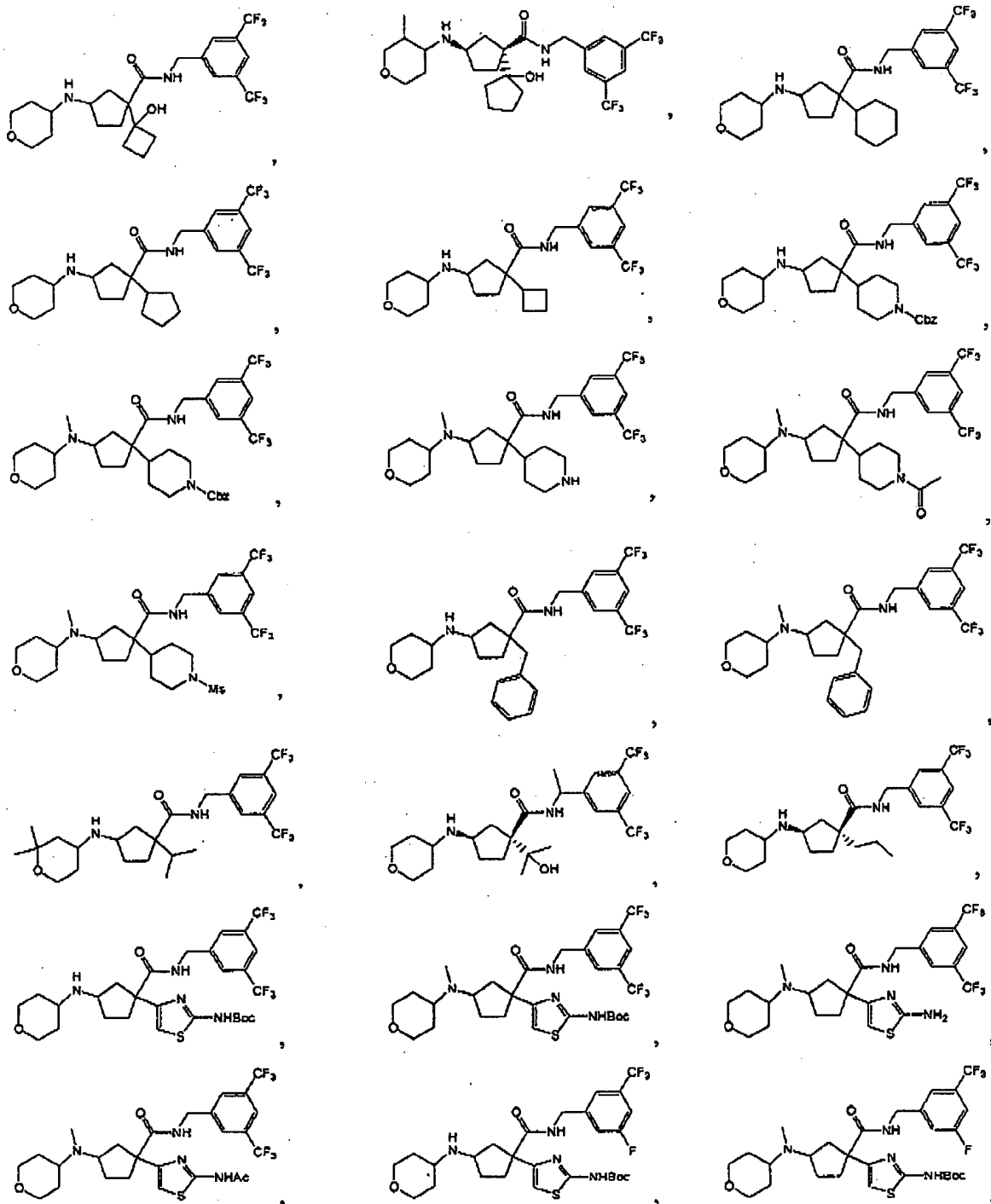
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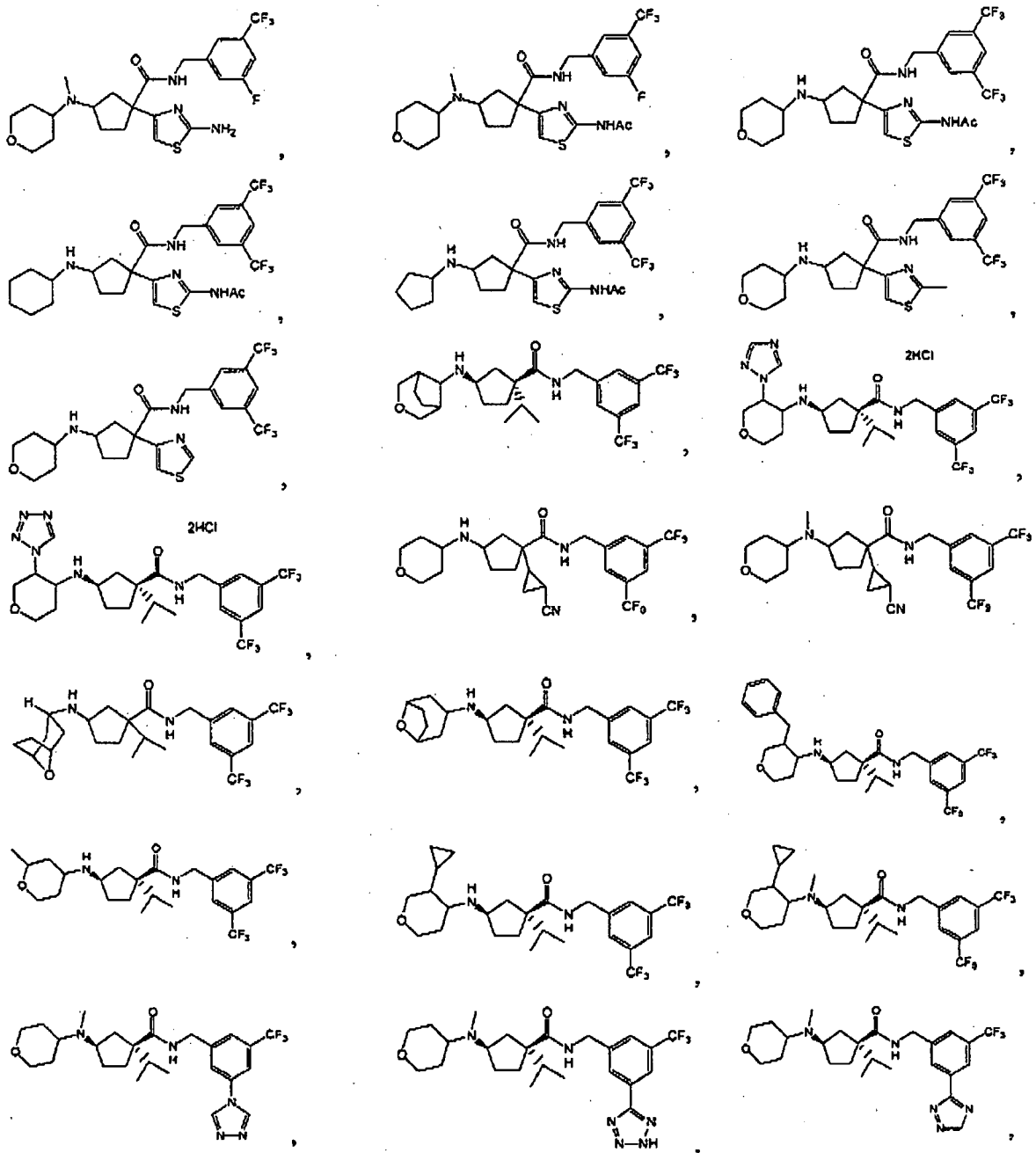


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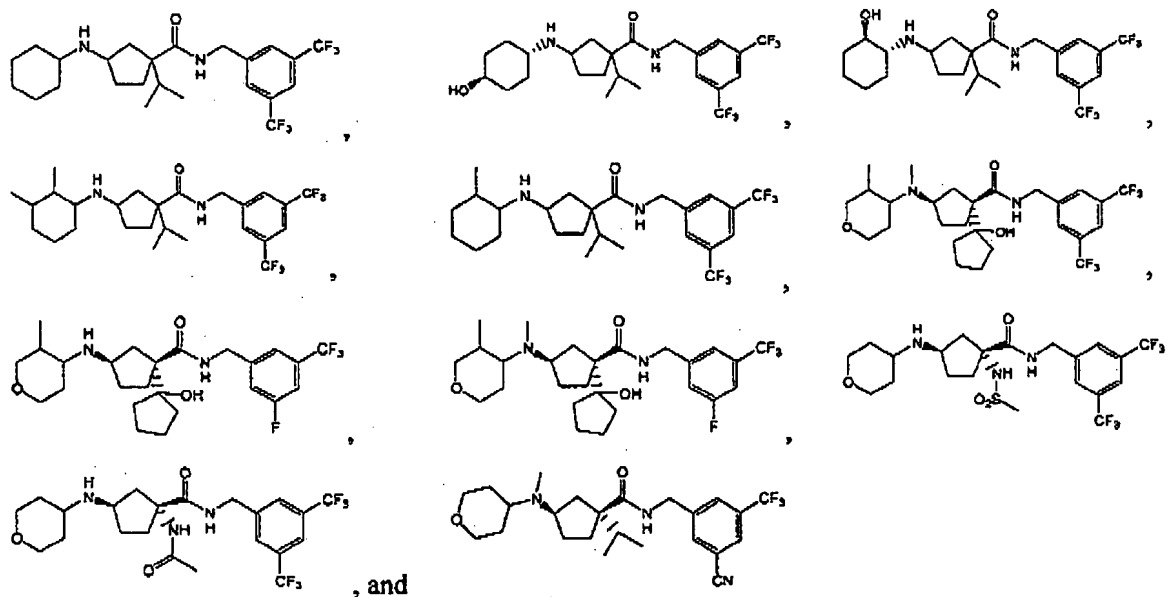
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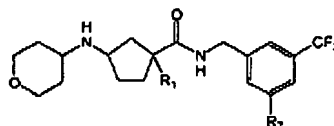
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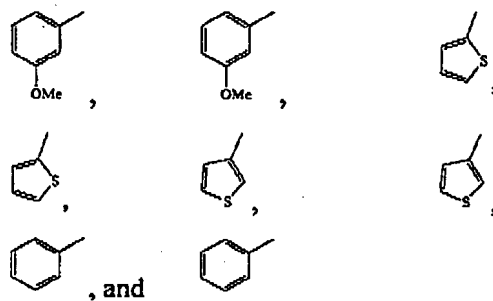


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

31. (previously presented) A compound of the formula:

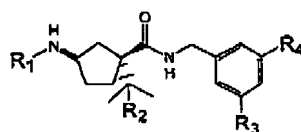



wherein R_7 is F or CF_3 , and wherein R_1 is selected from:

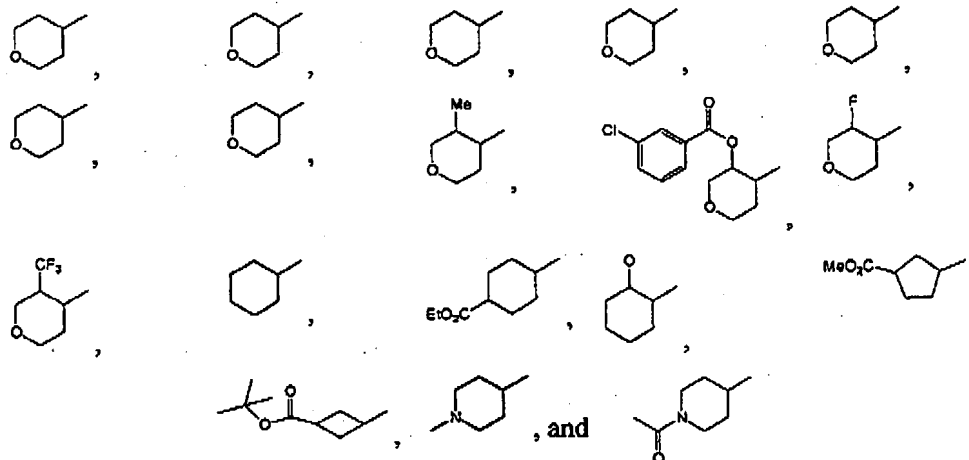


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

32. (previously presented) A compound of the formula:

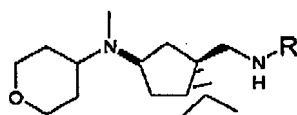


wherein R_2 is H or OH, wherein R_3 is F or CF_3 , wherein R_4 is CF_3 , Ph, OCF_3 , Cl, or , and wherein R_1 is selected from:



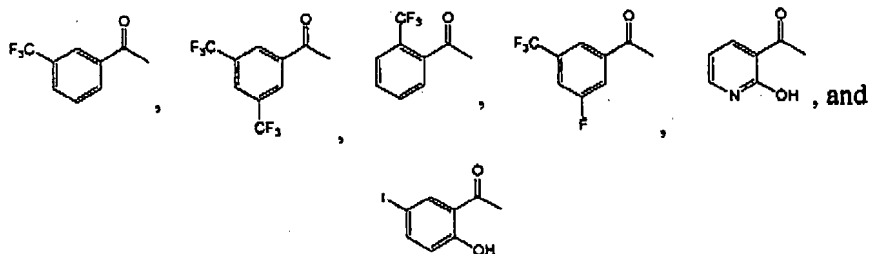
and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

33. (previously presented) A compound of the formula:



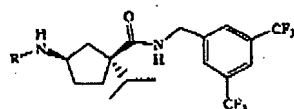
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wherein R is selected from:

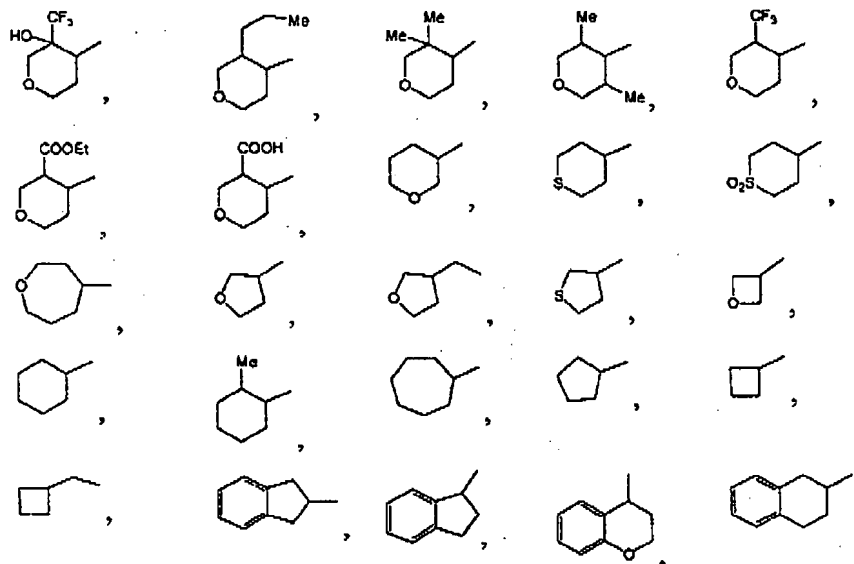


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

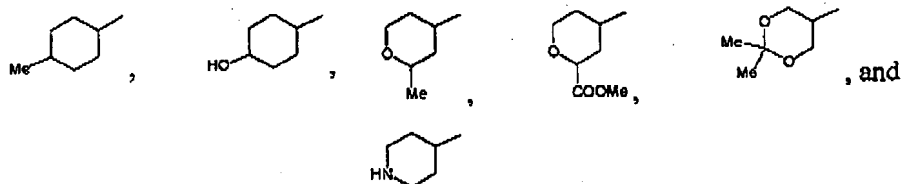
34. (previously presented) A compound of the formula:



wherein R is selected from:

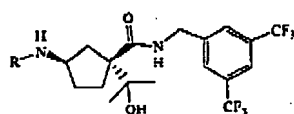


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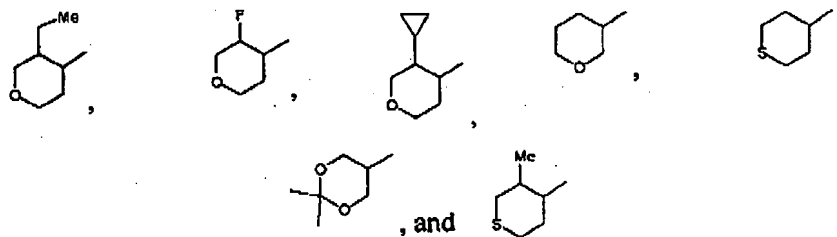


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

35. (previously presented) A compound of the formula:

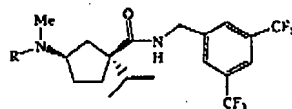


wherein R is selected from:

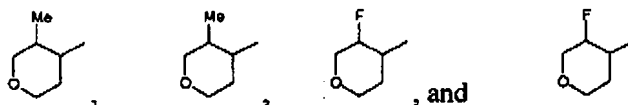


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

36. (previously presented) A compound of the formula:



wherein R is selected from:



and pharmaceutically acceptable salts thereof and individual diastereomers thereof.